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Effect of Vitamin D Supplementation on the Response of Phosphocalcic Metabolism in Moroccan Population

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Abstract

Vitamin D and calcium insufficiency is common among Moroccan people. Some recent data suggest that the use of moderate daily doses of vitamin D rather than high doses administered intermittently would be preferred. The aim of this work was to evaluate the impact of vitamin D supplementation on the response of phosphocalcic metabolism and on the correction of 25 (OH) D concentration in vitamin D insufficiency/deficiency/ normal individuals from Kenitra city (Morocco). We evaluated, from a randomized double-blind placebo-controlled study, the effects of daily administering of 600 IU of vitamin D3 for three months in 64 people, 32 people of normal weight and average age of 42 years and 32 obese people of average age of 48 years and having a normal concentration of vitamin D or presenting an insufficiency defined by serum concentrations of 25(OH)D ≤ 12 ng /ml. The mean patient age was 44 ± 7 years, no interaction was noted between weight status and vitamin D supplementation for measured calcium blood level in normal, overweight and obese participants ($p>0.05$). For phosphorus, a significant decrease has shown after vitamin D supplementation in individuals with normal weight ($P=0.008$), but without effect in overweight and obese individuals ($P> 0.05$). In individuals with normal vitamin D status, a reduction in 25 (OH) D plasma concentration was recorded in control normal participants with normal during the experience ($p<0.01$). But an increase of vitamin D plasma concentration was detected in vitamin D supplement group ($p=0.05$). Vitamin D supplementation increases the 25-OH-D plasma concentrations in normal ($p=0.001$), overweight ($p= 0.039$) and obese ($p=0.05$) participants. Supplementation in vitamin increases the level of vitamin D in individuals with deficiency in Vitamin D, and can be recommended for the population of Kenitra. Larger-scale and longer-term multicenter studies are needed to evaluate the clinical effects of such supplementation.

Keywords: Vitamin D deficiency; vitamin D supplementation; weight status; Morocco

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1. Introduction

Vitamin D is absorbed in the small intestine and synthesized in the skin. It is then transported to the liver to undergo a first transformation into 25 (OH) D to give the inactive form: 25 (OH) D or calcidiol. This hydroxylation is not regulated, the quantity synthesized and ingested increases the serum concentration of 25 (OH) D. Before this first hydroxylation, due to its lipid-soluble nature, part of the vitamin D can be stored in adipose tissue, especially if the subject is obese [1]. Vitamin D participates in the regulation of phosphocalcic metabolism and contributes to musculoskeletal health.

It stimulates the digestive absorption of calcium and phosphate and the expression of growth factors by the bone; it exerts a synergistic effect with parathyroid hormone (PTH), distal renal calcium reabsorption and bone remodeling, and exerts feedback control on PTH secretion. A profound vitamin D deficiency is responsible for pathologies characterized by a lack of bone mineralization and muscle pain [2]. Furthermore, various randomized trials against placebo have shown that vitamin D supplementation, generally associated with calcium, reduced the risk of non-vertebral fractures and reduced the risk of falls in the elderly provided that it provides at least 20 g (800 IU) of vitamin D

per day and that a 25OHD concentration of approximately 30 ng/mL is achieved. Another study showed that an optimal vitamin D status (25OHD concentration of at least 30ng/mL) was necessary for good anti-fracture effectiveness of anti-osteoporotic treatments [3]. The properties of vitamin D are dominated by its essential and complementary action to that of parathyroid hormone in the regulation of phosphocalcic metabolism. After its hydroxylation to 25-(OH) D at the liver level then to 1-25-(OH2) D at the kidney level, vitamin D is involved in the regulation of blood calcium, the mentalization of the skeleton, the homeostasis of phosphates; the three essential levels of action are: intestinal absorption, bone and kidney. More recently, other properties have been reported: immunomodulatory role, cell differentiation, modulation of secretions and hormonal syntheses including insulin [4].

Phosphocalcium metabolism is regulated mainly by the level of parathyroid hormone (PTH) secreted by the para-thyroid glands and vitamin D. Indeed, the secretion of PTH increases the concentration of blood Ca through its action on bone resorption and renal absorption and intestinal Calcium [5,6], while it reduces renal reabsorption of Phosphorus [7]. For its part, calcitriol (1,25(OH)2D3), the active form of vitamin D, stimulates intestinal absorption of Ca and P [8,9]. Calcitriol is also regulated by PTH secretion through negative feedback between these two hormones [9]. Several studies have shown the effectiveness of vitamin-calcium supplementation in reducing the incidence of peripheral fractures. This effect is mainly linked to an increase in Bone Mineral Density (BMD) associated with a reduction in parathyroid secretion accompanying vitamin D and calcium supplementation [10-11]. Also, a previous recent study performed by Baataoui et al. [12] has shown that a vitamin D deficiency is related to a lack of exercise, insufficient sun exposure, retention of blood vitamin D in adipose tissue and lower vitamin intake in the population of Kenitra (Morocco), and other studies on kenitra population have showed a low quality of life related to other diseases [13-16].

Due to the interest of such supplementation, it seemed important to us to evaluate the biological effects on phosphocalcic metabolism, as well as the changes in BMI during three months supplementation in vitamin D and calcium in a sample of Moroccan population in relation to weight and vitamin D status. The objective of this work was therefore to evaluate the impact of vitamin D supplementation on the response of phosphocalcic metabolism and on the correction of 25 (OH) D concentration in individuals with vitamin D insufficiency/deficiency/ normal from kenitra city.

2. Materials and Methods

2.1. Study design and population

A randomized double-blind placebo-controlled study was conducted, the effects of daily administration of 600 IU of vitamin D3, for three months in 32 people, 16 people of normal weight and average age of 42 years and 16 obese people of average age of 48 years and having a normal concentration of vitamin D or presenting an insufficiency defined by serum concentrations of 25(OH)D ≤ 12 ng /ml.

2.2. Supplementation protocol

Patients were randomized into two parallel groups to compare the effectiveness of daily vitamin D supplementation versus placebo. For this purpose, the patients received double-blind, for 3 months, 400 IU of vitamin D3 or a placebo. The patients receiving the supplement constitute the VitD group. The aim of this trial is to study the biological effects of vitamin D supplementation in these people. The patients gave their informed and written consent to participate in the trial.

2.3. Analysis of blood samples

The effect of the supplementation was evaluated by measuring biological parameters of phospho-calcium homeostasis: 25(OH)D, parathyroid hormone (PTH), serum calcium and phosphoremia at the beginning and at the end of the trial. Blood samples were taken in the morning on an empty stomach, the serum was collected then stored at –20°C. Serum calcium and phosphorus were measeaured by using COBAS e 411 automated Analyzer system (au-tomated system for immunological analyzes). The instrument uses electrochemiluminescence (ECL) technology to provide a wide variety of assays. Regarding the Vitamin D, PTH dosage: Using the MINI VIDAS automaton for the VIT D, PTH assay.

2.4. Statistical analysis

The main analysis was carried out on an intention-to-treat basis. The analysis of the evolution between the basal value and the end point is based on non-parametric tests due to the asymmetric distribution of the data according to Hodges-Lehmann method and Wilcoxon test [17]. The normal distribution of variables was assessed by Kolmogo-rov-Smirnov test. Serum calcium, PTH, phosphorus and 25 (OH) D were tested with both ANOVA. The post-hoc analyses were performed with Dunnett's test and Tukey's Honestly Significant Different (HSD) test. Differences were considered significant with $P < 0.05$ and trends with $P < 0.10$.

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3. Results and Discussions

3.1. Demographic and anthropometric characteristics of participants

The majority of participants are females (62.5%), aged between 30 and 39 years. According to weight status, 50% have normal weight (n=7), 18.7% are overweight (n=6) and 31.3% are obese (n=10). According to level study, 20 of participants have a primary school and 81% have a middle school level and above (table 1).

3.2. The effect of vitamin D supplementation on phosphocalcic parameters

The table 2 show the effects of 25 (OH) D3 supplementation on calcium, phosphorus, PTH and vitamin D blood levels. No interaction was noted between weight status and vitamin D supplementation for measured calcium blood level in normal, overweight and obese participants ($p>0.05$). For phosphorus, a significant decrease has shown after vitamin D supplementation in normal weight individuals (table 1, $P=0.008$), but without effect in overweight and obese individuals ($P> 0.05$). Vitamin D supplementation leads to a reduction in plasma concentrations of PTH in normal individuals. However, no effect was observed in overweight and obese participants ($P> 0.05$). The results show also that vitamin D supplementation increases the 25-OH-D plasma

concentrations in normal (p=0.001), overweight (p= 0.039) and obese (p=0.05) participants.

For all phosphocalcic parameters, no statistically significant differences was detected between normal, overweight and obese participants (p>0.05). Statistical significance for each weight status vs. vitamin D supplementation, or between conditions was indicated by asterisk(s). Two-tailed paired Student t-test P-values indicate the statistical significance (*P < 0.05, **P < 0.01, and **P < 0.001).

3.3. The effect of 25 (OH) D supplementation on vitamin D status

The figures 1, 2 and 3 show the effect of 25 (OH) D3 supplementation on vitamin D plasma concentrations on individuals with normal (figure 1), insufficiency (figure 2) and deficiency (figure 3) vitamin D. In individuals with normal vitamin D status (figure 1), a reduction in 25 (OH) D plasma concentration was recorded in control normal participants with normal during the experience (p<0.01). But an increase of vitamin D plasma con-centration was detected in vitamin D supplement group (p=0.05). In individuals with vitamin D insufficiency, also a reduction in 25 (OH) D plasma concentration was recorded in control individuals during the experience (p<0.01). However, no effect was observed in individuals with vitamin D insufficiency after supplementation (p>0.05). In vitamin D deficiency participants, no statistical difference in 25 (OH) D plasma concentration was detected in control group (p>0.05). But high statistical difference was observed in this group after vitamin d supplementation. In individuals with normal vitamin D status (figure 1), a reduction in 25 (OH) D plasma concentration was recorded in control normal participants with normal during the experience (p<0.01). But an increase of vitamin D plasma concentration was detected in vitamin D supplement group (p=0.05).

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Regarding anthropometric measurements, we did not find any significant effect related to weight status after vitamin D supplementation. This result agrees with that found by Al Sofiani et al. [18]. A previous study of Nikooyeh et al. [19] have shown a correlation between vitamin D administration and weight status. A link between vitamin D status and phosphocalcic metabolism has already been demonstrated by Le Thanh et al. (2015). The results show that people deficient in vitamin D responded better to daily supplementation with 25-OH-D3 with a dose of 400IU compared to normal people and people with vitamin D deficiency. These results, however, are the opposite of a reduction in PTH or an increase in calcitonin as shown in the table 2. In the present study, BMC was nevertheless not correlated with vitamin D status. In humans, calcitonin is known for its anti-resorptive effects by directly reducing osteoclast resorption leading to an increase in bone mineral density and bone strength [20]. In the same sense, a decrease in PTH reduces bone resorption. Less resorption could explain better mineralization.

There is general agreement that a daily intake of 400 IU of vitamin D can prevent nutritional rickets in infants and children [21]. However, the impact of vitamin D deficiency on the skeletal health of adults, especially those over 65 years old, and the potential non-skeletal effects of vitamin D are subjects of debate [22]. Some argue that supplementing with vitamin D is ineffective. On the contrary, others propose that the recommended vitamin D intake should be much higher than what the general population currently achieves. They suggest aiming for 25-hydroxyvitamin D (25OHD) concentrations comparable to those observed in certain equatorial African tribes with a sun exposure lifestyle resem-bling that of early humans [23-27]. Further studies will be necessary to evaluate the impact of Vitamin D supplementation on phosphocalcic metabolism. Analyzes of other blood parameters are in particular underway to try to elucidate the underlying mechanisms on phosphocalcic metabolism. The use of medicinal plant extract can be evaluated in the evolution of phosphocalcic metabolism in the response to vitamin D supplements as shown in other experimental studies [28,29]. Vitamin D supplementation did not result in significant improvement in phosphocalcic parameters as calcium and phosphorus in overweight and obese individuals. On the other hand, a significant increase of vitamin D level in patients with vitamin D deficiency. The metabolic effects of supplementation are still controversial, hence the need to expand studies to better demonstrate these effects.

Limitaions

Our work is the first in Morocco to have evaluated the effect of 25 (OH) D supplementation on phosphocalcic metabolism in patients in relation to weight and vitamin D status. However, this study has some limitations. First, the small number of participants and second, short period of follow up.

Table 1. Demographic and anthropometric characteristics of participants

Parameter	Number	Percentage (%)
Gender		
Female	40	62.5
Male	24	37.5
Age classes (years)		
20-29	14	21.9
30-39	26	40.6
40-49	18	28.1
50-59	6	9.4
Weight status		
Normal	32	50
Overweight	12	18.7
Obese	20	31.3
Level study		
Primary school	12	18.7
Middle school and higher	52	81.3
Family situation		
Single	16	25
Married	48	75

Table 2. Effects of 25 (OH) D3 supplementation on phosphocalcic parameters in participants

	Before			After			P value	
Weight status	**Normal**	**Overweight**	**Obese**	**Normal**	**overweight**	**obese**	**Weight status**	**Vit D supp**
Calcium (mg/l)	94.84±4.95	94.80±3.67	93.09±6.64	94.09±4.58	93.82±2.98	92.04±6.80	0.342	0.102
Phosphorus (mg/l)	37.13±9.06	36.63±5.99	38.54±7.50	34.44±7.65*	36.22±4.03	31.15±4.83	0.228	0.302
PTH (pg/ml)	66.93±15.26	81.78±28.11	55.51±18.18	54.28±13.65**	65.68±18.40	53.84±9.90	0.153	0.173
Vitamin D (mg/ml)	21.02±7.09	24.92±8.19	18.66±7.07	24.37±7.20***	28.9±8.31*	23.58±5.13**	0.426	0.015

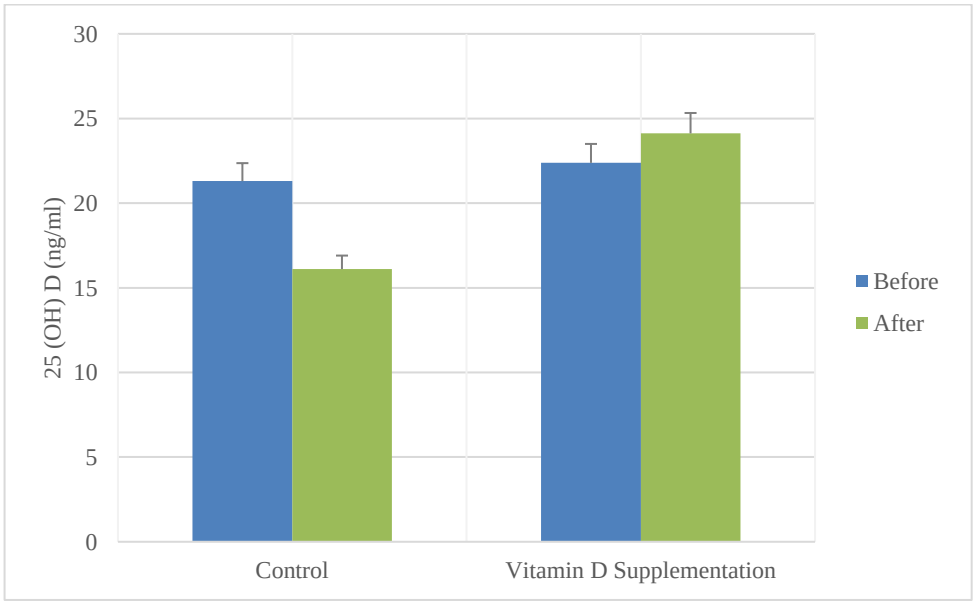

Figure 1. Impact of vitamin D supplementation in participants with Vitamin D insufficiency

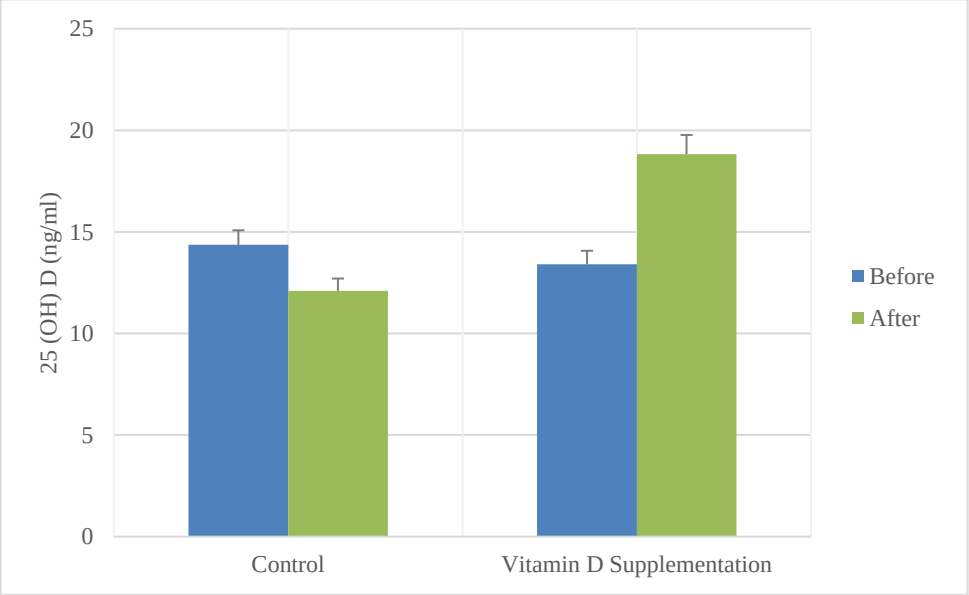

Figure 2. Impact of vitamin D supplementation in vitamin D status in participants with Vitamin D deficiency

4. Conclusions

The use of moderate daily doses of vitamin D rather than high doses administered intermittently would be preferred in subjects with deficiency. Further studies will be necessary to better understand the role of vitamin D supplementation on phosphocalcic and vitamin D metabolism. Therefore, a study is planned to evaluate changes in phosphocalcic metabolism in sample of Moroccan during fasting Ramadan. Larger studies could confirm our results and demonstrate the benefits of vitamin D supplementation in deficient patients.

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